Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology
Office of Pharmacovigilance and Epidemiology

Pediatric Postmarketing Pharmacovigilance Review

Date:	November 7, 2023
Reviewer:	Ivone Kim, MD, Medical Officer Division of Pharmacovigilance I
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Product Name:	Primatene Mist (epinephrine) aerosol for inhalation
Pediatric Labeling Approval Date:	November 7, 2018
Application Type/Number:	NDA 205920
Applicant:	Armstrong Pharmaceuticals, Inc.
TTT Record ID:	2023-6436

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EXECUTIVE SUMMARY

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Primatene Mist (epinephrine) aerosol for inhalation in pediatric patients less than 18 years of age. The Division of Pharmacovigilance (DPV) conducted this review in accordance with the Pediatric Research Equity Act (PREA). This review focuses on serious unlabeled adverse events associated with Primatene Mist in pediatric patients.

Primatene Mist (epinephrine) aerosol for inhalation (NDA 205920) containing hydrofluoroalkane propellant is a non-selective (alpha and beta-2) adrenergic receptor agonist that was initially approved in the U.S. on November 7, 2018. Primatene Mist is available as a metered-dose-inhaler (MDI) currently indicated for the temporary relief of mild symptoms of intermittent asthma (including wheezing, tightness of chest, shortness of breath) in adults and children 12 years of age and older. At approval, NDA 205920 became the only MDI approved for nonprescription use. Nonprescription Primatene Mist is approved only for those patients who have been diagnosed with asthma by a health care provider and it is not considered a replacement for prescription asthma treatments.

Of note another Primatene Mist product, NDA 016126, containing chlorofluorocarbon was initially approved on November 8, 1967, for the temporary relief of shortness of breath, tightness or chest, and wheezing due to bronchial asthma. NDA 0616126 was withdrawn from the market per the Federal Register effective June 18, 2009.

This pediatric postmarketing safety review was prompted by pediatric labeling at initial approval for Primatene Mist (NDA 205920), that included use in pediatric patients aged 12 years and older. The safety and effectiveness of Primatene Mist have not been established for children younger than 12 years. A pediatric postmarketing pharmacovigilance review for Primatene Mist has not been previously presented to the Pediatric Advisory Committee.

DPV reviewed all serious FAERS reports with Primatene Mist in pediatric patients less than 18 years of age from November 7, 2018 – September 18, 2023, and identified one report. However, DPV excluded the report from further discussion.

There were no new safety signals identified, no increased severity or frequency of any labeled adverse events, and no deaths directly associated with Primatene Mist in pediatric patients less than 18 years of age.

DPV did not identify any new pediatric safety concerns for Primatene Mist at this time and will continue routine pharmacovigilance monitoring for Primatene Mist.

1 INTRODUCTION

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Primatene Mist (epinephrine) aerosol for inhalation in pediatric patients less than 18 years of age. The Division of Pharmacovigilance (DPV) conducted this review in accordance with the Pediatric Research Equity Act (PREA). This review focuses on serious unlabeled adverse events associated with Primatene Mist in pediatric patients.

1.1 PEDIATRIC REGULATORY HISTORY

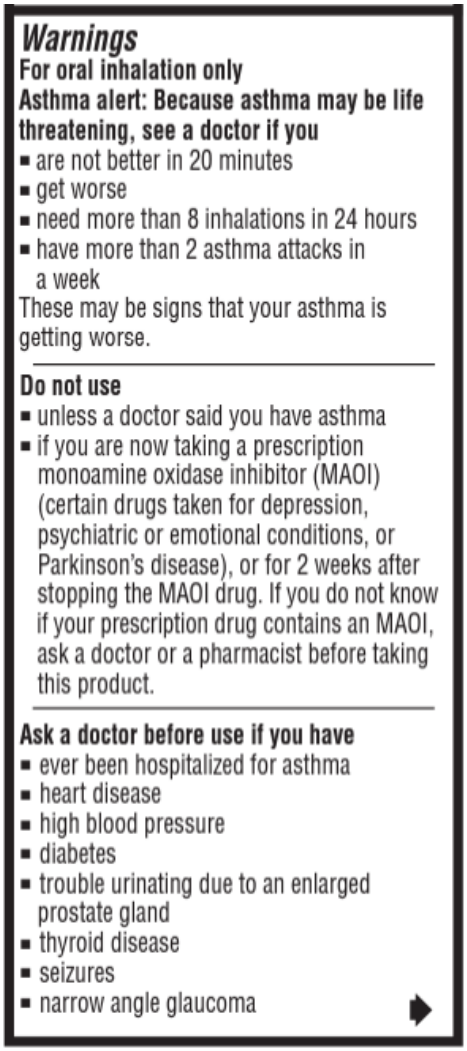
Primatene Mist (epinephrine) aerosol for inhalation (NDA 205920) containing hydrofluoroalkane propellant is a non-selective (alpha and beta-2) adrenergic receptor agonist that was initially approved in the U.S. on November 7, 2018. Primatene Mist is available as a metered-dose-inhaler (MDI) currently indicated for the temporary relief of mild symptoms of intermittent asthma (including wheezing, tightness of chest, shortness of breath) in adults and children 12 years of age and older.[1] At approval, NDA 205920 became the only MDI approved for nonprescription use.[2] Nonprescription Primatene Mist is approved only for those patients who have been diagnosed with asthma by a health care provider and it is not considered a replacement for prescription asthma treatments.

Of note another Primatene Mist product, NDA 016126, containing chlorofluorocarbon was initially approved on November 8, 1967, for the temporary relief of shortness of breath, tightness or chest, and wheezing due to bronchial asthma. NDA 016126 was withdrawn from the market per the Federal Register effective June 18, 2009.[3]

This pediatric postmarketing safety review was prompted by pediatric labeling at initial approval for Primatene Mist (NDA 205920), that included use in pediatric patients aged 12 years and older. The safety and effectiveness of Primatene Mist have not been established for children younger than 12 years. A pediatric postmarketing pharmacovigilance review for Primatene Mist has not been previously presented to the Pediatric Advisory Committee.

1.2 RELEVANT LABELED SAFETY INFORMATION

The Primatene Mist labeling contains the following safety information reproduced from the nonprescription Drug Facts label. For additional Primatene Mist labeling information, please refer to the nonprescription Drug Facts label.[1]



Warnings

For oral inhalation only

Asthma alert: Because asthma may be life threatening, see a doctor if you

- are not better in 20 minutes
- get worse
- need more than 8 inhalations in 24 hours
- have more than 2 asthma attacks in a week

These may be signs that your asthma is getting worse.

Do not use

- unless a doctor said you have asthma
- if you are now taking a prescription monoamine oxidase inhibitor (MAOI) (certain drugs taken for depression, psychiatric or emotional conditions, or Parkinson's disease), or for 2 weeks after stopping the MAOI drug. If you do not know if your prescription drug contains an MAOI, ask a doctor or a pharmacist before taking this product.

Ask a doctor before use if you have

- ever been hospitalized for asthma
- heart disease
- high blood pressure
- diabetes
- trouble urinating due to an enlarged prostate gland
- thyroid disease
- seizures
- narrow angle glaucoma

2 METHODS AND MATERIALS

2.1 FAERS SEARCH STRATEGY

DPV searched the FAERS database with the strategy described in **Table 1**.

Table 1. FAERS Search Strategy*	
Date of search	September 19, 2023
Time period of search	November 7, 2018 – September 18, 2023
Search type	Drug Safety Analytics Dashboard (DSAD) Quick Query
Product terms	Product Name: Primatene Mist NDA: 205920
MedDRA search terms (Version 26.0)	All Preferred Terms
* See Appendix A for a description of the FAERS database † Primatene Mist NDA 205920 U.S. approval date Abbreviations: MedDRA=Medical Dictionary for Regulatory Activities, NDA=New Drug Application	

3 RESULTS

3.1 FAERS

3.1.1 Total Number of FAERS Reports by Age

Table 2 presents the number of adult and pediatric FAERS reports through September 18, 2023, with Primatene Mist.

Table 2. Total Adult and Pediatric FAERS Reports* Received by FDA From November 7, 2018 – September 18, 2023, With Primatene Mist

	All Reports (U.S.)	Serious† (U.S.)	Death (U.S.)
Adults (≥ 18 years)	54 (51)	8 (8)	1 (1)
Pediatrics (0 - < 18 years)	3 (3)	1 (1)	0 (0)

* May include duplicates and transplacental exposures, and have not been assessed for causality

† For the purposes of this review, the following outcomes qualify as serious: death, life- threatening, hospitalization (initial or prolonged), disability, congenital anomaly, required intervention, or other serious important medical events.

3.1.2 Selection of Serious Pediatric Cases in FAERS

Our FAERS search retrieved one serious pediatric report from November 7, 2018 – September 18, 2023. We reviewed the pediatric report with a serious outcome. We excluded the report from the case series as it contained insufficient information to interpret the adverse event.

3.1.3 Summary of Fatal Pediatric Cases (N=0)

There are no fatal pediatric adverse event cases for discussion.

3.1.4 Summary of Serious Non-Fatal Pediatric Cases (N=0)

There are no non-fatal pediatric adverse event cases for discussion.

4 DISCUSSION

DPV reviewed all serious FAERS reports with Primatene Mist in pediatric patients less than 18 years of age from November 7, 2018 – September 18, 2023, and identified one report. However, DPV excluded the report from further discussion.

There were no new safety signals identified, no increased severity or frequency of any labeled adverse events, and no deaths directly associated with Primatene Mist in pediatric patients less than 18 years of age.

5 CONCLUSION

DPV did not identify any new pediatric safety concerns for Primatene Mist at this time and will continue routine pharmacovigilance monitoring for Primatene Mist.

6 REFERENCES

1. Primatene Mist (epinephrine) aerosol for inhalation. [Drugs Facts Label]. Canton, MA; Armstrong Pharmaceuticals, Inc.: 2018.

2. Food and Drug Administration. FDA statement on approval of OTC Primatene Mist to treat mild asthma. Available at: https://www.fda.gov/news-events/press-announcements/fda-statement-approval-otc-primatene-mist-treat-mild-asthma. Accessed on September 19, 2023.

3. Federal Register. Vol 74, No 95. Tuesday, May 19, 2009. (2009-N-0211)

7 APPENDICES

7.1 APPENDIX A. FDA ADVERSE EVENT REPORTING SYSTEM (FAERS)

The FDA Adverse Event Reporting System (FAERS) is a database that contains information on adverse event and medication error reports submitted to FDA. The database is designed to support FDA's postmarketing safety surveillance program for drug and therapeutic biological products. The informatic structure of the database adheres to the international safety reporting guidance issued by the International Council on Harmonisation. Adverse events and medication errors are coded to terms in the Medical Dictionary for Regulatory Activities terminology. The suspect products are coded to valid tradenames or active ingredients in the FAERS Product Dictionary.

FAERS data have limitations. First, there is no certainty that the reported event was actually due to the product. FDA does not require that a causal relationship between a product and event be proven, and reports do not always contain enough detail to properly evaluate an event. Further, FDA does not receive reports for every adverse event or medication error that occurs with a product. Many factors can influence whether an event will be reported, such as the time a product has been marketed and publicity about an event. Therefore, FAERS data cannot be used to calculate the incidence of an adverse event or medication error in the U.S. population.

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